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09/942,935	08/31/2001	Brigitte Bathe	32301WD216	8953

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SMITH, GAMBRELL & RUSSELL, LLP
SUITE 800
1850 M STREEt, N.W.
WASHINGTON, DC 20036

EXAMINER	
KERR, KATHLEEN M	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 11/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/942,935	BATHE ET AL.	
	Examiner	Art Unit	
	Kathleen M Kerr	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *13-27,29 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *03/20/02* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Application Status

1. In response to the previous Office action, a written restriction requirement (mailed on June 4, 2003), Applicants filed an election received on June 18, 2003. Claims 1-30 are pending in the instant Office action.

Election

2. Applicants' election of Group I, Claims 1-12 and 28 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (M.P.E.P. § 818.03(a)).

The requirement is deemed proper and is therefore made FINAL.

Claims 1-30 are pending in the instant Office action. Claims 11-27 and 29-20 are withdrawn from further consideration as non-elected inventions. Claims 1-12 and 28 will be examined herein.

Priority

3. The instant application is granted the benefit of priority for the foreign applications 100 43 337.5 and 101 36 984.0 filed in Germany on September 2, 2000 and July 28, 2001, respectively as requested in the declaration. Receipt is acknowledged of papers submitted under 35 U.S.C. § 119(a)-(d), which papers have been placed of record in the file. Said papers are not in English and thus, cannot be used to provide evidence of an earlier effective filing date for the pending claims. Thus, the earliest effective filing date for the pending claims is August 31, 2001 in the instant Office action.

Information Disclosure Statement

4. The information disclosure statement filed on March 20, 2002 has been reviewed, and its references have been considered as shown by the Examiner's initials next to each citation on the attached copy. The search report has been reviewed but is crossed out on the IDS since it is not printed on the face of a patent.

The Examiner notes that documents EP 1108790 and Beggs *et al.* were filed without an accompanying IDS. The mere filing of copies does not guarantee their consideration.

Declaration

5. The Examiner notes that the declaration filed December 10, 2001 has the box checked "attached hereto" concerning the specification; however the specification was previously filed on August 31, 2001. This is considered a typographical error since the title and inventors names match that filed on August 31, 2001; the declaration is adequate for the instant application. No action is required by Applicants.

Sequence Compliance

6. By virtue of the sequence listing filed on December 10, 2001 listing 4 sequences and the statement under 37 C.F.R. § 1.821(f), the instant application fully complies with the sequence rules.

Objections to the Specification

7. In the specification, the Abstract is objected to for not completely describing the disclosed subject matter (see M.P.E.P. § 608.01(b)). It is noted that in many databases and in

foreign countries, the Abstract is crucial in defining the disclosed subject matter, thus, its completeness is essential. The Examiner suggests the inclusion of the full name of the protein, sigma factor M activity, and the source species, *Corynebacterium glutamicum,* for completeness.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-4, 6-8, and 28 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 1, the phrase "from coryneform bacteria" is unclear as to its metes and bounds. Does this phrase limit the claimed polynucleotides to those native to coryneform? Or can any polynucleotide that can be found in coryneform, recombinantly or otherwise (i.e., an *E. coli* gene can be on a plasmid transformed into coryneform) read on the claim? Clarification is required. The Examiner suggests the term ---native to--- for clarity.

9. Claims 1-4, 6-8, and 28 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "coding for the sigM gene" is unclear. Firstly, a polynucleotide sequence does not "coding for" a gene; polynucleotides are genes that code for (or encode) polypeptides. Thus, this limitation is unclear. Secondly, which *sigM* gene is intended? The term "**the** sigM gene" (emphasis added) indicates a particular *sigM* gene, for example SEQ ID NO:1; however, tremendous breadth of structure in the claimed genus follows

this term. Thirdly, items c and d are wholly unclear considering any encoding limitation since item c is drawn to the complement of a coding sequence and d is drawn to small fragments. Thus, the metes and bounds of the instant claims are unclear.

10. Claim 2 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "sigma factor M activity" is unclear. What kind of activity is it? Is it an enzyme, a receptor? The specification offers no description of the term either directly or by reference. Thus, the metes and bounds of the term are wholly unclear. Clarification is required.

11. Claim 7 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "further comprising ... sense mutations that are neutral in terms of function" is unclear. Since a DNA's function is to encode a protein, does this phrase mean within the degeneration of the genetic code (already claimed in Claim 6, item ii)? Or is the retention of the function of the encoded protein intended? The phrase is wholly unclear. Moreover, must the DNA of Claim 6 also have this limitation or is it another option to be added to Claim 6 as implied by the item number "iv"? If it is another option added, Claim 7 does not further limit the parent claim appropriately. Clarification is required.

12. Claims 10-11 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "**the** sigM gene" (emphasis added) indicates a particular *sigM*

gene; however, the breadth of the claims is unclear. Must the coryneform's own sigM gene be enhanced? And must that be by an identical copy of sigM (i.e., is a *C. glutamicum* sigM sufficient to enhance sigM in *C. diphtheriae* or must the *C. diphtheriae* sigM be used)? Clarification is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 1-4, 6-8, and 28 are rejected under 35 U.S.C. 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 1-4, 8 and 28 are drawn to polynucleotides having a particular structure without any clear function. Claims 6-7 require no particular structure due to the breadth of "hybridizes" in Claim 6, item iii, and no particular function.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which

is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

The instant specification discloses polynucleotides encoding polypeptides with at least 70% identity with SEQ ID NO: 2. Applicants have described a genus relating to said SEQ ID NO with both sequence identity limitations and functional limitations (i.e., having sigma factor M activity). However, the genus of the instant claims also contains polynucleotides within the sequence identity limitations, but having different function. Moreover, based on the unclear functional limitation in Claim 2, this claim is also included in the instant rejection. Additionally, no description of polynucleotides derived "from coryneform" is found to the exclusion of any sigM gene to adequately describe the claimed subgenus. Applicants have not fully described a genus that has sequence identity limitations in the absence of clear functional limitations.

14. Claims 10-11 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 10 is drawn to bacterium having enhanced sigM gene that is claimed solely by function and without any structural limitations.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

In the instant specification, genes encoding sigM are briefly described as having been obtained from *Corynebacterium glutamicum*. These genes are only described according to the functional characteristics of the enzymes they encode; no structural relationship is described or used in the claims. Thus, one of skill in the art would be unable to predict the structure of other members of this genus by virtue of the instant disclosure. Therefore, claims drawn to bacteria containing the genus of said genes are also not adequately described. The Examiner suggests inserting structural and, if necessary, functional language into the claims to describe the sigM gene to be enhanced.

15. Claims 1-4, 6-8, 10-11, and 28 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for any polynucleotide encoding

SEQ ID NO:2 (a sigM gene), does not reasonably provide enablement for polynucleotides encoding polypeptides having as little as 70% identity with SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. To make the claimed product commensurate with the claimed scope would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

The instant specification teaches SEQ ID NO:2, a sigma factor protein from *C. glutamicum*, and SEQ ID NO:1, a *C. glutamicum* gene exactly encoding SEQ ID NO:2. The art

includes no examples of sigM encoding genes. The art fully enables any DNA encoding SEQ ID NO:2 based on the degeneracy of the genetic code. While the instant specification describes and enables means for identifying other sigM genes using hybridization methods, etc., these methods do not enable one of skill in the art to make all, or a relevant portion of, the polynucleotide products within the scope of the claims because the ability to find a sigM gene, which is structurally related to SEQ ID NOs:1 and/or 2, is not equivalent to the ability to make a sigM gene as required by the statute (i.e., "make and use"). No description in the specification or the art provides particular residues whose encoding is important within the disclosed sequence so that its sigM-nature is maintained. Thus, one of skill in the art would be unable to predict the structure of the other members of the genus in order to make such members. Therefore, the instant claims are not enabled to the full extent of their scope.

16. Claims 10-11 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for coryneform comprising an overexpression vector containing the sigM gene (a polynucleotide encoding SEQ ID NO:2), does not reasonably provide enablement for any sigM gene that is enhanced and/or overexpressed in coryneform by other means as described in the specification. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. To make the claimed product commensurate with the claimed scope would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized above.

The instant specification teaches a sigM gene from *C. glutamicum* and transformation techniques used for coryneform host cell. Thus, one of skill in the art could readily produce expression vectors of the disclosed gene for overexpression in *C. glutamicum*. However, the claimed scope also includes using altered sigM genes such that the gene was enhanced or overexpressed (i.e., changing RNA transcript stability, protein stability, etc., see paragraphs {0023] and [0039]). No examples, guidance, or direction is presented to enable one of skill in the art to produce such host cells. Moreover, it is wholly unpredictable how to produce such sigM genes for overexpression. Thus, the instant claims are not fully enabled.

17. Claim 12 is rejected under 35 U.S.C. § 112, first paragraph, enabling deposit, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. To practice the instant methods, one of skill in the art is required to have DSM 14409, which is disclosed as containing pEC-XK99EsigMalex, or is required to have all the components to produce pEC-XK99EsigMalex. The components are not readily available, and the deposit fails to fully enable the claims. While the instant specification contains limited deposit information, the requirements to enable such a deposit have not been fully met by the instant application. To enable the instant claims by enabling the deposit of DSM 14409, the following items are required: (1) the accession number assigned by the depository, (2) the date of deposit, (3) a brief description of the deposit, (4) the name and **full address** of the depository (37 C.F.R. § 1.801 - 1.809) (those which are in bold have not been fulfilled by the instant specification), and (5) the record must also contain a statement certifying that all restrictions on accessibility to said deposit be irrevocably removed by Applicant upon the granting of the patent

(see M.P.E.P. § 2404.01); this statement may be certified by Applicants or Applicants' representative.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 1-3, 6-8, and 28 are rejected under 35 U.S.C. § 102(a) as being anticipated by Pompejus *et al.* (WO 01/00843). The instant claims are drawn to polynucleotides that are fragments of a nucleic acid encoding SEQ ID NO:2 and *C. glutamicum* that overexpress the sigM gene.

Pompejus *et al.* teach SEQ ID NO:507 (3005-3075 bp) that matches SEQ ID NO:1 from 1-71 bp (see attached alignment). Pompejus *et al.* also teach overexpression of SEQ ID NO:507 in *C. glutamicum* to produce lysine using overexpression vectors (see page 8).

19. Claims 1-11 and 28 are rejected under 35 U.S.C. § 102(a) as being anticipated by Nakagawa *et al.* (EP 1108790). The instant claims are drawn to polynucleotides similar to a nucleic acid encoding SEQ ID NO:2 and *C. glutamicum* that overexpress the sigM gene.

Nakagawa *et al.* teach SEQ ID NO:7069, a portion of which (299357-300567 bp) is equivalent to SEQ ID NO:1 (1-1211 bp). Nakagawa *et al.* also teach overexpression of the disclosed sequences in *C. glutamicum* to produce the encoded polypeptides (see page 22).

20. Claims 1-3 and 6-8 are rejected under 35 U.S.C. § 102(b) as being anticipated by Zhao *et al.* (GenBank Accession Number AZ241095. RPCI-23-35N21.TV RPCI-23 Mus musculus genomic clone RCPI-23-35N21, genomic survey sequence. June 15, 2000). The instant claims are drawn to DNA sequences having at least 15 consecutive nucleotides of SEQ ID NO:1 and that hybridize to SEQ ID NO:1.

Zhao *et al.* teach a mouse DNA sequence that comprises, from 251-232 bp, an identical sequence to that of SEQ ID NO:1 (905-924) (see attached alignment). Limitations to encoding a sigM gene are unclear, as noted above.

Other Relevant Art

21. The following is cited to complete the record for the reasons noted:

a) Amador *et al.* Structure and organization of the *rrnD* operon of '*Brevibacterium lactofermentum*': analysis of the 16S rRNA gene. Microbiology (1999) 145: 915-924.

Conclusion

22. Claims 1-11 and 28 are rejected for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229. The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

KMK
October 29, 2003